PATENT SPECIFICATION

655,198

Date of Application and filing Complete Specification: May 10, 1948.

No. 12805/48.

Application made in United States of America on Sept. 30, 1947.

Complete Specification Published: July 11, 1951.

Index at acceptance:—Classes 1(i), F12; 23, N, X; and 81(i), B11b8.

COMPLETE SPECIFICATION

Process and Apparatus for the Irradiation of Liquids

We, ALLIED LABORATORIES, INC., a corporation duly organized under the laws of the State of Delaware, United States of America, of 406, West 34th Street, Kansas City, State of Missouri, United States of America, do hereby declare the nature of this invention and in what manner the same is to be performed, to be particularly described and ascertained in and by the following statement:—

The present invention relates to the treatment of liquids with radiant energy. Particularly, it relates to a process and apparatus for producing a thin, continuously flowing film of a liquid and subjecting said film of liquid to the action of radiant energy. Still more particularly, it relates to the use of centrifugal force for producing a thin continuously flowing film of a liquid over a relatively large surface area and subjecting said film to the action of ultraviolet radiation.

In the past, it has been known that a thin film of liquid could be subjected to the action of ultraviolet radiation and that such treatment would kill the microorganisms and/or viruses present in the liquid. In spite of the fact that the sterilizing action of ultraviolet radiations on liquid food and medicinal substances is known, it has not been as widely used commercially as is desired. One of the principal reasons for the apparent lack of wide commercial use of ultraviolet radiations for sterilizing liquids is the difficulty of producing films of the liquid substances thin enough to permit adequate penetration of the radiations. Another reason why the prior art conditions are not entirely satisfactory for volume production is that the quantity of liquid flowed in a thin film past an effective ultraviolet light source has been very limited. Of course, some are used in commercial processing operations but it is extremely desirable that the output and efficiency be increased.

In accordance with the present invention, we have provided a process and apparatus for more efficiently producing thin films of liquid while simultaneously subjecting said films to the action of radiant energy. Our improved apparatus utilizes a process which broadly comprises a method of employing centrifugal force for maintaining a uniformly thin continuously flowing film of liquid and in such a manner that the thin film can be subjected to action of ultraviolet radiations to produce effective sterilization or killing of the microorganisms and/or viruses present in the liquid.

It is an advantage of this invention that an efficient process and a relatively inexpensive apparatus is provided for sterilizing or killing microorganisms and/or virus present in liquids.

It is also an advantage of this invention that relatively large volumes of liquid can be irradiated by our improved process in a relatively short period of time.

An additional advantage is that a new and improved process is provided for irradiating a wide variety of liquids.

A further advantage of the present invention is that it permits the utilization of the readily available low pressure resonance ultraviolet lamp.

An outstanding advantage of our invention is its usefulness for the commercial production of potent vaccines and antigens.

An additional outstanding advantage is its use for sterilizing antiserums, antitoxins, aggressins and other biological products.

A further outstanding advantage is that the surface on which the thin film of liquid is produced is sterilized by the ultraviolet radiations.

The above enumerated and other advantages of our invention will become apparent during the course of the following description.

The accompanying drawing illustrat-

[P.

ing our apparatus is a central vertical section of the apparatus.

As illustrated, the apparatus comprises a cylinder 1, which can be a stainless steel open ended tube about 30 inches long and about 2 inches in diameter, suspended by ball bearings 2 mounted on a supporting frame 3. The cylinder 1 also has mounted thereon a pulley 4 grooved for a V-belt so it can be driven by a constant speed motor (not shown) or other suitable source of power.

A 30 W. germicidal ultraviolet (commercially available) lamp 5 is positioned vertically inside the cylinder 1 and spaced so that the ultraviolet radiations are effectively transmitted to the inside cylinder wall. A lamp socket 7 is positioned in a support 6 in such a manner that when the lamp 5 is plugged in as shown, it is positioned axially to the cylinder 1. An upper lamp socket 9 is supported by a member 8 directly above the socket 7 and also in the vertical center of the cylinder 1. A support member 8 is removably attached to the frame support 3 in order that the lamp can be inserted in the lower socket 7 and then the member 8 and socket 9 placed in an operative position. Sockets 7 and 9 are connected to a constant electric power source (not shown). A liquid collecting cup 10 has an opening in the center thereof to permit the lamp 5 to pass through, an inner wall which extends some distance up and around the lamp 5 and an outer wall around the cylinder 1 being spaced therefrom and extending some distance up the wall of said cylinder. The conduit or space between the inner and outer walls of the cup 10 serves to collect liquid which can be discharged through the spout shown thereon. The cup 10 is held in the desired position by thumb screws 11 as illustrated. A cylindrical member 12 is attached to the lower side of the pulley 4 and extends over and around the outer wall of the collecting cup 10 to serve as a dust guard therefor.

A container 13 has an air inlet 14 and a liquid outlet tube 15. The liquid outlet tube 15 terminates with a liquid feed on needle 16, the terminal outlet of which is positioned near the inside wall of the cylinder 1. Hypodermic needles have been found to be satisfactory as feed on needles since the rate of liquid flow can be altered by simply using needles of different gauge. A support member 17 serves to support the liquid feed on needle 16 and permits adjustment thereof.

In utilizing our apparatus, illustrated in the drawing, for carrying out our process the liquid to be irradiated is placed in the container 13 the air inlet tube attached to a constant air pressure source and the liquid thus forced at a constant rate through the feed on device 16. The cylinder 1 is rotated at a constant speed by means of a constant speed motor through a V-belt around the pulley 4. The speed of rotation must be fast enough to centrifugally produce a thin film of the liquid along the inner wall. The ultraviolet lamp 5 having been previously positioned as shown in the drawing is connected with a constant electric power source as indicated. The inner wall of the cylinder is sterilized by the radiations prior to the introduction of the liquid. The previously sterilized liquid collecting cup 10 also is positioned as illustrated in the drawing.

The tip of the feed on needle 16 is positioned relative to the inner wall of cylinder 1 and direction of rotation so as to flow the liquid on to the cylinder without splashing. As the liquid is fed on to the inner wall of the rotating cylinder 1 it flows downward and because of the centrifugal force of the rotating cylinder forms a thin film of liquid over the entire inner surface of the cylinder. The thin film of liquid as it flows down the cylinder wall is subjected to the action of the radiations from the ultraviolet lamp 5. The irradiated liquid is collected in the liquid collecting cup 10 as it flows from the lower end of the cylinder and thence out the spout into a suitable receptacle. The upper open end of the rotating cylinder is protected from the atmosphere by a formalin soaked piece of gauze or other suitable means.

The following examples will serve to illustrate the present invention.

EXAMPLE I.

STERILIZATION OF LIQUID SUSPENSION OF E. COLI.

A suspension of E. Coli from a 24 hour growth on nutrient agar was adjusted to contain 300 million organisms per cc. as determined by plate count.

Approximately 600 cc. samples of the suspension were fed onto the inner wall of the 2 inch cylinder, through different gauge hypodermic needles while the cylinder was rotated at 1140 R.P.M. A constant pressure of 14.5 cm. of mercury was used to deliver the suspension to the cylinder and the speed of flow onto the cylinder being varied by using increasing sizes (gauges) of hypodermic needles at the outlet.

The 30 watt germicidal lamp located axially to the rotating cylinder furnished a constant source of ultraviolet radiations and by varying the rate of flow of the suspension, the time of irradiation was easily controlled.

The following table gives results obtained in a series of runs.

Lot No.	Needle Gauge No.	Volume of Suspension cc.	Total flow time minutes	Rate of Flow cc. per minute	Per Cent E. Coli Killed
1	24	600	40	15	100
2	22	625	23	27	100
3	20	625	12	52	100
4	18	620	7	89	100

It is obvious that at the rates of flow illustrated in the table the irradiated E. coli suspensions were completely sterilized. A further series of runs were made with the E, coli suspensions and it was found that the maximum speed of irradiation to ensure sterility with the apparatus was approximately 250 cc. per minute.

Example II.

INACTIVATION OF RABIES VIRUS IN GOAT BRAIN TISSUE.

A 10% suspension of goat brain infected with rabies virus was made by mixing 388 gms. of brain with 3.492 cc. of physiological saline solution in a colloid mill. The resulting suspension was filtered through 325 mesh bolting silk to remove particulate matter. A sample was drawn and the presence of living virus demonstrated.

Several batches of the material were irradiated as described in Example 1 using 1140 R.P.M. for the cylinder speed and 13.9 cm. of pressure on the liquid. The rate of flow of the various batches was altered by using different gauge needles.

The results are summarized in the following table.

Batch No.	Needle Gauge No.	Volume of Suspension cc.	Total flow time Minutes	Rate of Flow cc. per minute	Degree of Inactivation
1	24	600	51	12	Complete
2	22	600	25.5	24	Complete
3	20	600	11	55	Complete
4	18	600	6	100	Complete
5	16	600	3.5	218	Complete

The virus in all of the irradiated samples was proven to be inactivated by inoculating mice intercerebrally with 0.03 cc. doses with no resulting deaths.

Example III.

INACTIVATION OF EQUINE ENCEPHALOMYELITIS VIRUS.

In similar experiments a total of about 800 cc. of Equine Encephalomyelitis virus 33 and ½% chick embryo suspension was inactivated at €, 26, 57 and 153 cc. per minute rates of flow respectively.

Example IV.

INACTIVATION OF MINK DISTEMPER VIRUS.

A total of about 1000 cc. of a 5% suspension of mink distemper virus infected ferret spleen was satisfactory inactivated by irradiating at rates of flow of 100 and 117 and 135 cc. per minute respectively.

Example V.

HUMAN RABIES VACCINE PRODUCTION.

365 grams of rabies infected rabbit brain tissue was ground in a colloid mill with 3285 cc. of physiological saline solution to give 10% tissue suspension and filtered through bolting silk. The suspension was irradiated at a rate of 133 cc. per minute using 14.5 cm. mercury pressure and an 18 gauge needle to regulate the flow.

The irradiated vaccine passed the

standard sterility and potency tests, and was marketed as Human rabies Vaccine Serial #212,013.

The following lots of Human Rabies Vaccine were all produced using different times of irradiation as indicated.

Serial No.	Quantity cc.	Irradiated at rate of flow cc. per minute
212015	5550	150
212016	3350	280
212017	3200	160
212018	3000	220
212019	4000	240
212020	3500	230
212021	3400	130
212022	3200	250

The above vaccines all passed the standard sterility and potency tests prescribed for commercial rabies vaccines.

Example VI.

Sterilization of serums contaminated with bacteria.

The following commercial quantities of serums contaminated with bacteria of various kinds were successfully sterilized. The antigenicity of the serums was not impaired by treatment.

The rate of flow (i.e. time of irradiation) for each serum was determined by processing a small quantity and testing for sterility and activity after which the large quantity was processed. The time of irradiation varied with the different products as was expected, but in nearly all cases the time of irradiation could be varied considerably and good results still obtained.

1. Anti-Swine Erysipelas Serum—632,000 cc.

2. Anti - Hemorrhagic - Septicemia Serum, Bovine Origin—45,000 cc.

3. Corynebacterium Pasteurella-Pseudodiphthericum, Bovina, Origin—88,000 cc.

4. Antibacterial Serum Canine, Equine Origin #2—91,000 cc.

5. Anti - Bacterial Serum Equine, Equine Origin #1—18,000 cc.

6. Anthrax Serum, Bovine Origin—70,000 cc.

7. Anthrax Serum, Equine Origin—12,000 cc.

8. Anti-Anthrax Serum, Bovine Origin—32,000 cc.

9. Anti - Equine Encephalomyelitis Serum, Equine Origin—18,000 cc.

Example VII.

Sterilization of antigens.

The following commercial quantities of antigens contaminated with bacteria were successfully sterilized. In both cases, the antigens retained their full biologic values.

1. Tuberculin - 16,000 cc.
2. Mallein - - 2,000 cc.

It is to be understood that the above examples are for illustrative purposes only and that the present invention is not limited thereto. In the specific examples, the apparatus employed comprised a rotatable stainless steel tube having a diameter of 2 inches and 30 inches long and a 30 w. germicidal lamp having a diameter of 1 inch and 36 inches long. Therefore, the distance the radiations traveled to contact the rotating inner wall of the cylinder was a constant and the time of irradiation was easily controlled by varying the rate of introduction of the liquid onto the cylinder wall.

The thickness of the liquid film was varied by varying the rate of introduction of the liquid on to the cylinder wall as well as by varying the speed of rotation of the cylinder from about 1140 to 1750 R.P.M.

The character of the liquid being irradiated determines to a large extent what conditions of irradiation must be used. A viscuous liquid would require introduction at a relatively slower rate than a non-viscuous one and a different speed or rotation of the cylinder in order to produce a continuous film of suitable thinness for irradiation. Liquids possessing biological activity as a general rule would require preliminary tests to determine the best condition for treatment of each substance. Relatively inert liquids contaminated with microorganisms could on the other hand perhaps be sterilized over a wider range of conditions.

The type of stainless steel cylinder employed is readily available commercially and is preferred but the cylinder could be composed of any other rigid substance such as, for example, aluminium, magnesium, glass, etc. Likewise, the diameter of the cylinder may be varied so long as the thin film of liquid is spaced an effective distance from the radiation source.

The 30 w. germicidal lamp 2537Å unit wave length employed is likewise readily available and a preferred one. The 15 w. commercially available germicidal tubular lamps are also satisfactory. Our in-

vention, however, may utilize radiations from any type source known to produce a desired effect on a liquid in the form of a thin film so long as it can be arranged relative to our centrifugally produced thin film of liquid to permit the radiation action to take effect on the liquid. For example, the lamp could be of the high pressure type ultraviolet emitting lamp. Radio active substances suitably positioned may also be employed.

The ultraviolet radiations of 2537Å are preferred when we are concerned with inactivating, killing, attenuating or otherwise altering microorganisms or viruses, such as in vaccine production. In other cases, we may use radiations of different Å units for special purposes where such other Å units are known to be particularly desirable. For example, in the production of Vitamin D and in carrying out chemical reactions, we would use a radiation source having a high percentage of radiations in the desired range.

In our specific apparatus illustrated, the lamp is shown positioned inside and longitudinally (i.e. axially) to the rotatable cylinder and is our preferred arrangement.

In operation of our apparatus and process, the cylinder rotating at the relatively high rate of speed is air cooled and prevents the liquid from being overheated. In the case of solid substances which are stable to and liquified by heat, we may heat the cylinder to maintain a fluid condition during irradiation. It is obvious that we can thus easily control the temperature of the liquid being irradiated.

We have previously pointed out that the 2 inch diameter rotatable tube may be replaced by one of either a smaller or larger diameter so long as the ray source is positioned an effective distance from the thin film of liquid. In other instances a shorter tube may likewise be used to reduce the time of irradiation. To increase volume or time of irradiation, longer tube or tubes in series may be employed. In the case of tubes having a very large diameter several of the 30 w. germicidal lamps may be arranged within the inner periphery of the tube and spaced an effective distance therefrom. Reflectors may be used to good advantage in some cases also.

It is apparent from the foregoing description and illustration that our process of utilizing centrifugal force for producing a thin film of liquid and especially a uniformly continuously flowing thin film of liquid while simultaneously subjecting said film to the action of radiations has real commercial merit and differs materially from the previously proposed processes.

Having now particularly described and ascertained the nature of our said invention and in what manner the same is to be performed, we declare that what we claim is:—

1. A process for irradiating liquids with active rays, including the steps of rapidly rotating a vertical tubular member, introducing the liquid to be treated against the upper area of the inside wall of said member, producing a downwardly flowing uniformly thin film on the inner surface of said member by means of centrifugal force due to said rotating, and maintaining said film with centrifugal force while treating the same with said active rays, said rays emanating from a source arranged within said tubular member.

2. A process for irradiating liquids. as set forth in claim 1, including the step of controlling the rate at which the liquid is introduced into the interior of the rapidly rotating tubular member.

3. A process for irradiating liquids, as set forth in claims 1 and 2, in which the irradiation of the liquid is carried out with ultraviolet rays.

4. A process for irradiating liquids, as set forth in claim 3, in which the ultraviolet irradiation is applied to liquids containing micro-organisms and/or viruses.

5. A process for irradiating liquids, as set forth in claims 1 and 3, in which the irradiation with ultraviolet rays is carried out on infective liquid substance for producing vaccines therefrom.

6. A process for irradiating liquids, as set forth in claim 1, in which the film produced by centrifugal force is subjected to the action of ultraviolet irradiation of essentially 2537Å.

7. An apparatus for irradiating liquids by the process set forth in claim 1, including a rotatable cylinder in substantially vertical position, with means for directing a liquid onto the upper inner wall of the cylinder, and a source of irradiating light extending axially through the entire vertical cylinder.

8. An apparatus as set forth in claim 7, including means for directing measured quantities of a liquid onto the inner wall of the cylinder.

9. An apparatus, as set forth in claims 7 and 8, in which an ultraviolet lamp emitting radiations of principally 2537Å constitutes the source of irradiation.

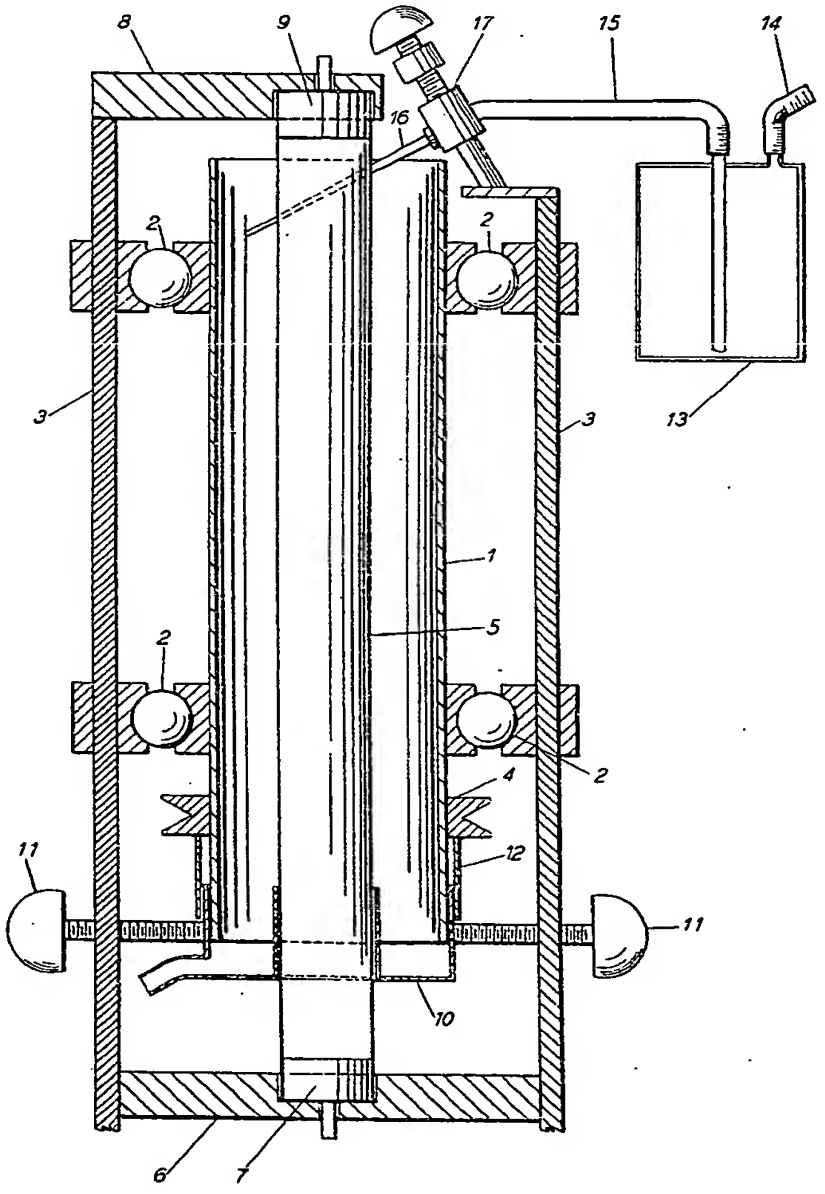
10. A process for irradiating liquids, substantially as described, and for the purpose set forth.

11. An apparatus for irradiating

liquids substantially as described and shown, and for the purpose set forth.

Dated this 10th day of May, 1948.
For the Applicant,
FRANK B. DEHN & CO.,
Chartered Patent Agents,
Kingsway House, 103, Kingsway,
London, W.C.2.

Leamington Spa: Printed for His Majesty's Stationery Office, by the Courier Press.—1951.
Published at The Patent Office, 25, Southampton Buildings, London, W.C.2, from which copies, price 2s. per copy; by post 2s. 1d. may be obtained.



H.M.S.O. (M.F.P.)